

**WHAT IS CLAIMED IS:**

1. A method of identifying a polynucleotide or pattern of polynucleotides regulated by one or more sepsis or inflammatory inducing agents and inhibited by a cationic peptide comprising contacting the polynucleotide or polynucleotides with one or more sepsis or inflammatory inducing agents, contacting the polynucleotide or polynucleotides with a cationic peptide either simultaneously or immediately thereafter, and determining a change in expression, wherein a change is indicative of a polynucleotide or pattern of polynucleotides that is regulated by a sepsis or inflammatory inducing agent and reduced by a cationic peptide.
2. The method of claim 1, wherein the sepsis or inflammatory inducing agent is LPS, LTA or CpG DNA, bacterial components or whole cells, or related agents.
3. The method of claim 1, comprising determining the level of expression of the polynucleotide prior to and following contacting with the sepsis or inflammatory inducing agent.
4. A polynucleotide or polynucleotide pattern identified by the method of claim 1.
5. A polynucleotide of claim 3, wherein the polynucleotide encodes a polypeptide involved in an inflammatory or septic response.
6. A method of identifying an agent that blocks sepsis or inflammation comprising combining a polynucleotide of claim 5 with an agent, wherein expression of the polynucleotide in the presence of the agent is modulated as compared with expression in the absence of the agent and wherein the modulation in expression affects the inflammatory or septic response.
7. The method of claim 6, wherein the effect is inhibition of the inflammatory or septic response.
8. An agent identified by the method of claim 6.

9. The agent of claim 8, wherein the agent is a peptide, peptidomimetic, chemical compound, nucleic acid molecule or a polypeptide.
10. The agent of claim 8, wherein the peptide is selected from SEQ ID NO:4-54.
11. A method of identifying a pattern of polynucleotide expression for inhibition of an inflammatory or septic response comprising:
  - contacting cells with LPS, LTA, CpG DNA and/or intact bacteria or bacterial components in the presence or absence of a cationic peptide;
  - detecting a pattern of polynucleotide expression for the cells in the presence and absence of the peptide, wherein the pattern in the presence of the peptide represents inhibition of an inflammatory or septic response.
12. The method of claim 11, further comprising contacting cells with one or more compounds suspected of inhibiting an inflammatory or septic response and identifying a compound that provides a pattern of polynucleotide expression similar to a pattern obtained with a cationic peptide that inhibits an inflammatory or septic response.
13. A compound identified by the method of claim 11.
14. A method of identifying an agent that enhances innate immunity comprising:
  - contacting a polynucleotide or polynucleotides that encode a polypeptide involved in innate immunity, with an agent of interest, wherein expression of the polynucleotide in the presence of the agent is modulated as compared with expression of the polynucleotide in the absence of the agent and wherein the modulated expression results in enhancement of innate immunity.
15. The method of claim 14, wherein the agent does not stimulate a septic reaction.
16. The method of claim 14, wherein the agent inhibits the inflammatory or septic response.

17. The method of claim 14, wherein the agent blocks the inflammatory or septic response.
18. The method as in any of claims 16 or 17, wherein the agent increases the expression of an anti-inflammatory encoding polynucleotide.
19. The method of claim 18, wherein the anti-inflammatory gene is selected from a subset that includes IL-1 R antagonist homolog 1 (AI167887), IL-10 R beta (AA486393), IL-10 R alpha (U00672), TNF Receptor member 1B (AA150416), TNF receptor member 5 (H98636), TNF receptor member 11b (AA194983), IK cytokine down-regulator of HLA II (R39227), TGFB inducible early growth response 2 (AI473938), CD2 (AA927710), glucocorticoid-related polynucleotides (AK000892), or IL-10 (M5762720).
20. The method of claim 19, wherein the agent inhibits the expression of TNF-alpha.
21. The method of claim 19, wherein the agent inhibits the expression of interleukins.
22. The method of claim 23, wherein the interleukin is IL-8.
23. The method of claim 16, wherein the agent is a peptide.
24. The method of claim 23, wherein the peptide is selected from SEQ ID NO:4-54.
25. An agent identified by the method of claim 14.
26. An agent of claim 25, wherein the agent is a peptide, peptidomimetic, chemical compound, or a nucleic acid molecule.
27. A method of identifying a pattern of polynucleotide expression for identification of a compound that selectively enhances innate immunity comprising:
  - detecting a pattern of polynucleotide expression for cells contacted in the presence and absence of a cationic peptide, wherein the pattern in the presence of the peptide represents stimulation of innate immunity;
  - detecting a pattern of polynucleotide expression for cells contacted in the presence of a test compound, wherein a pattern with the test compound that is similar to

the pattern observed in the presence of the cationic peptide, is indicative of a compound that enhances innate immunity.

28. A compound identified by the method of claim 27.
29. The method of claim 27, wherein the compound does not stimulate a septic reaction.
30. The method of claim 27, wherein the polynucleotide expression pattern includes expression of pro-inflammatory polynucleotides.
31. The method of claim 30, wherein the pro-inflammatory polynucleotides include ring finger protein 10 (D87451), serine/threonine protein kinase MASK (AB040057), KIAA0912 protein (AB020719), KIAA0239 protein (D87076), RAP1, GTPase activating protein 1 (M64788), FEM-1-like death receptor binding protein (AB007856), cathepsin S (M90696), hypothetical protein FLJ20308 (AK000315), pim-1 oncogene (M54915), proteasome subunit beta type 5 (D29011), KIAA0239 protein (D87076), mucin 5 subtype B tracheobronchial (AJ001403), cAMP response element-binding protein CREBPa, integrin alpha M (J03925), Rho-associated kinase 2 (NM\_004850), PTD017 protein (AL050361) unknown genes (AK001143, AK034348, AL049250, AL16199, AL031983), retinoic acid receptor (X06614), G protein-coupled receptors (Z94155, X81892, U52219, U22491, AF015257, U66579) chemokine (C-C motif) receptor 7 (L31584), tumor necrosis factor receptor superfamily member 17 (Z29575), interferon gamma receptor 2 (U05875), cytokine receptor-like factor 1 (AF059293), class I cytokine receptor (AF053004), coagulation factor II (thrombin) receptor-like 2 (U92971), leukemia inhibitory factor receptor (NM\_002310), interferon gamma receptor 1 (AL050337) or any combination thereof.
32. The method of claim 27, wherein the expression pattern includes expression of polynucleotides encoding chemokines.
33. The method of claim 27, wherein the expression pattern includes expression of cell differentiation factors.

34. The method of claim 27, wherein the polynucleotide expression pattern includes expression of cell surface receptors.

35. The method of claim 34, wherein the cell surface receptors include chemokine receptors or integrin receptors.

36. A method of identifying an agent that is capable of selectively enhancing innate immunity comprising:

contacting a cell containing a polynucleotide or polynucleotides that encode a polypeptide involved in innate immunity, with an agent of interest, wherein expression of the polynucleotide or polynucleotides in the presence of the agent is modulated as compared with expression in the absence of the agent and wherein the modulated expression results in enhancement of innate immunity.

37. The method of claim 26 in which the pattern of expression is utilized in screening for compounds that enhance innate immunity.

38. A compound of claim 28, wherein the compound stimulates chemokine or chemokine receptor expression.

39. A compound of claim 38, wherein the chemokine or chemokine receptor is CXCR4, CCR5, CCR2, CCR6, MIP-1 alpha, IL-8, MCP-1, MCP-2, MCP-3, MCP-4, or MCP-5.

40. A compound of claim 28, wherein the compound is a peptide, peptidomimetic, chemical compound, or a nucleic acid molecule.

41. A method of identifying an agent that is capable of both suppressing or blocking septic or inflammatory responses and enhancing innate immunity comprising:

contacting a cell containing i) a polynucleotide or polynucleotides that encode a polypeptide capable of suppressing inflammatory or septic responses and ii) a polynucleotide or polynucleotides that encode a polypeptide involved in innate immunity,

with an agent of interest, wherein expression of in the presence of the agent is modulated as compared with expression of the polynucleotide or polynucleotides in the absence of the agent and wherein the modulated expression results in suppression of inflammatory or septic responses and enhancement of innate immunity.

42. A method for inferring a state of infection in a mammalian subject from a nucleic acid sample of the subject comprising identifying in the nucleic acid sample a polynucleotide expression pattern exemplified by an increase in polynucleotide expression of at least 2 polynucleotides in Table 55 as compared to a non-infected subject.

43. A method for inferring a state of infection in a mammalian subject from a nucleic acid sample of the subject comprising identifying in the nucleic acid sample a polynucleotide expression pattern exemplified by a decrease in polynucleotide expression of at least 2 polynucleotides in Table 56 as compared to a non-infected subject.

44. A method for inferring a state of infection in a mammalian subject from a nucleic acid sample of the subject comprising identifying in the nucleic acid sample a polynucleotide expression pattern exemplified by a polynucleotide expression of at least 2 polynucleotides in Table 57 as compared to a non-infected subject.

45. The method of any of claims 30, 31 or 32, wherein the state of infection is due to a bacteria, virus, fungus or parasitic agent.

46. The method of any of claims 30, 31 or 32, wherein the state of infection is due to a Gram positive or Gram negative bacteria.

47. A polynucleotide expression pattern of a subject having a state of infection identified by the method of claim 31.

48. A cationic peptide that is an antagonist of CXCR-4.

49. A method of identifying a cationic peptide that is an antagonist of CXCR-4 comprising contacting T cells with SDF-1 in the presence of absence of a test peptide

and measuring chemotaxis, wherein a decrease in chemotaxis in the presence of the test peptide is indicative of a peptide that is an antagonist of CXCR-4.

50. An isolated cationic peptide comprising the general formula

$X_1X_2X_3IX_4PX_5X_2X_1$  (SEQ ID NO: 4), wherein  $X_1$  is one or two of R, L or K,  $X_2$  is one of C, S or A,  $X_3$  is one of R or P,  $X_4$  is one of A or V and  $X_5$  is one of V or W.

51. The cationic peptide of claim 38, wherein the peptide is selected from the group consisting of: LLCRIVPVIPWCK (SEQ ID NO: 5), LRCPIAPVIPVCKK (SEQ ID NO: 6), KSRIVPAIPVSL (SEQ ID NO: 7), KKSPIAPAIPWSR (SEQ ID NO: 8), RRARIVPAIPVARR (SEQ ID NO: 9) and LSRIAPAIPWAKL (SEQ ID NO: 10).

52. The peptide of claim 38, wherein the peptide has anti-inflammatory activity.

53. The peptide of claim 38, wherein the peptide has anti-sepsis activity.

54. An isolated cationic peptide comprising the general formula

$X_1LX_2X_3KX_4X_2X_5X_3PX_3X_1$  (SEQ ID NO: 11), wherein  $X_1$  is one or two of D, E, S, T or N,  $X_2$  is one or two of P, G or D,  $X_3$  is one of G, A, V, L, I or Y,  $X_4$  is one of R, K or H and  $X_5$  is one of S, T, C, M or R.

55. The cationic peptide of claim 42, wherein the peptide is selected from the group consisting of: DLPAKRGSA PGST (SEQ ID NO: 12), SELPGLKHPCVPGS (SEQ ID NO: 13), TTLGPVKRDSIPGE (SEQ ID NO: 14), SLPIKHDRLPATS (SEQ ID NO: 15), ELPLKRGRVPVE (SEQ ID NO: 16) and NLPDLKKPRVPATS (SEQ ID NO: 17).

56. The peptide of claim 42, wherein the peptide has anti-inflammatory activity.

57. The peptide of claim 42, wherein the peptide has anti-sepsis activity.

58. An isolated cationic peptide comprising the general formula

$X_1X_2X_3X_4WX_4WX_5K$  (SEQ ID NO: 18), wherein  $X_1$  is one to four chosen from A, P or R,  $X_2$  is one or two aromatic amino acids (F, Y and W),  $X_3$  is one of P or K,  $X_4$  is one, two or none chosen from A, P, Y or W and  $X_5$  is one to three chosen from R or P.

59. The cationic peptide of claim 46, wherein the peptide is selected from the group consisting of: RPRYPWWPWPYRPRK (SEQ ID NO: 19), RRAWWKAWWARRK (SEQ ID NO: 20), RPYWPWAWARPRK (SEQ ID NO: 21), RPAWKYWWPWPWPRRK (SEQ ID NO: 22), RAAFKWAWAWWRRK (SEQ ID NO: 23) and RRRWKWAWPRRK (SEQ ID NO: 24).
60. The peptide of claim 46, wherein the peptide has anti-inflammatory activity.
61. The peptide of claim 46, wherein the peptide has anti-sepsis activity.
62. An isolated cationic peptide comprising the general formula  $X_1X_2X_3X_4X_1VX_3X_4RGX_4X_3X_4X_1X_3X_1$  (SEQ ID NO: 25) wherein  $X_1$  is one or two of R or K,  $X_2$  is a polar or charged amino acid (S, T, M, N, Q, D, E, K, R and H),  $X_3$  is C, S, M, D or A and  $X_4$  is F, I, V, M or R.
63. The cationic peptide of claim 50, wherein the peptide is selected from the group consisting of: RRMCIKVCVRGVCRRKCRK (SEQ ID NO: 26), KRSCFKVSMRGVSRRRCK (SEQ ID NO: 27), KKDAIKKVDIRGMDMRRAR (SEQ ID NO: 28), RKMVKVDVRGIMIRKDRR (SEQ ID NO: 29), KQCVKVAMRGMALRRCK (SEQ ID NO: 30) and RREAIRRVAMRGRDMKRMRR (SEQ ID NO: 31).
64. The peptide of claim 50, wherein the peptide has anti-inflammatory activity.
65. The peptide of claim 50, wherein the peptide has anti-sepsis activity.
66. An isolated cationic peptide comprising the general formula  $X_1X_2X_3X_4X_1VX_5X_4RGX_4X_5X_4X_1X_3X_1$  (SEQ ID NO: 32), wherein  $X_1$  is one or two of R or K,  $X_2$  is a polar or charged amino acid (S, T, M, N, Q, D, E, K, R and H),  $X_3$  is one of C, S, M, D or A,  $X_4$  is one of F, I, V, M or R and  $X_5$  is one of A, I, S, M, D or R.
67. The cationic peptide of claim 54, wherein the peptide is selected from the group consisting of: RTCVKRVAMRGIIRKRCR (SEQ ID NO: 33), KKQMMKRVDYRGISVKRKR (SEQ ID NO: 34), KESIKVIIRGMMVRMCK (SEQ



ID NO: 35), RRDCRRVMVRGIDIKAK (SEQ ID NO: 36),  
KRTAIKKVSRRGMSVKARR (SEQ ID NO: 37) and RHCIRRVSMRGIIMRRCK  
(SEQ ID NO: 38).

68. The peptide of claim 54, wherein the peptide has anti-inflammatory activity.

69. The peptide of claim 54, wherein the peptide has anti-sepsis activity.

70. An isolated cationic peptide comprising the general formula  
KX<sub>1</sub>KX<sub>2</sub>FX<sub>2</sub>KMLMX<sub>2</sub>ALKKX<sub>3</sub> (SEQ ID NO: 39), wherein X<sub>1</sub> is a polar amino acid (C,  
S, T, M, N and Q); X<sub>2</sub> is one of A, L, S or K and X<sub>3</sub> is 1-17 amino acids chosen from G,  
A, V, L, I, P, F, S, T, K and H.

71. The cationic peptide of claim 58, wherein the peptide is selected from the group  
consisting of: KCKLFFKKMLMLALKKVLTTGLPALKLTK (SEQ ID NO: 40),  
KSKSFLKMLMKALKKVLTTGLPALIS (SEQ ID NO: 41),  
KTKKFAKMLMMALKKVVSTAKPLAILS (SEQ ID NO: 42),  
KMKSFAKMLMLALKKVLKVLTTALTALKAGLPS (SEQ ID NO: 43),  
KNKAFAKMLMKALKKVTAAKPLTG (SEQ ID NO: 44) and  
KQKLFAKMLMSALKKKTLVTTPLAGK (SEQ ID NO: 45).

72. The peptide of claim 58, wherein the peptide has anti-inflammatory activity.

73. The peptide of claim 58, wherein the peptide has anti-sepsis activity.

74. An isolated cationic peptide comprising the general formula  
KWKX<sub>2</sub>X<sub>1</sub>X<sub>1</sub>X<sub>2</sub>X<sub>2</sub>X<sub>1</sub>X<sub>2</sub>X<sub>2</sub>X<sub>1</sub>X<sub>1</sub>X<sub>2</sub>X<sub>2</sub>IFHTALKPISS (SEQ ID NO: 46), wherein X<sub>1</sub> is a  
hydrophobic amino acid and X<sub>2</sub> is a hydrophilic amino acid.

75. The cationic peptide of claim 62, wherein the peptide is selected from the group  
consisting of: KWKSFLRTFKSPVRTIFHTALKPISS (SEQ ID NO: 47),  
KWKSYAHTIMSPVRLIFHTALKPISS (SEQ ID NO: 48),  
KWKRGAHRFMKFLSTIFHTALKPISS (SEQ ID NO: 49),  
KWKKWAHSPRKVLTRIFHTALKPISS (SEQ ID NO: 50),

KWKSLVMMFKKPARRIFHTALKPISS (SEQ ID NO: 51) and  
KWKHALMKAHMLWHMIFHTALKPISS (SEQ ID NO: 52).

76. The peptide of claim 62, wherein the peptide has anti-inflammatory activity.

77. The peptide of claim 62, wherein the peptide has anti-sepsis activity.

78. An isolated cationic peptide comprising the sequence  
KWKSFLRTFKSPVRTVFHTALKPISS (SEQ ID NO: 53).

79. An isolated cationic peptide comprising the sequence  
KWKSYAHTMSPVRLVFHTALKPISS (SEQ ID NO: 54).

80. The method of claim 28, wherein the agent is a Zinc finger protein (AF061261); Cell cycle gene (S70622); IL-10 Receptor U00672); Transferase (AF038664); Homeobox protein (AC004774); Forkhead protein (AF042832); Unknown (AL096803); KIAA0284 Protein (AB006622); Hypothetical Protein (AL022393); Receptor (AF112461); Hypothetical Protein (AK002104); Protein (AL050261); Polypeptide (AF105424); SPR1 protein (AB031480); Dehydrogenase (D17793); Transferase (M63509); and Peroxisome factor (AB013818).

81. The polynucleotide expression pattern of a subject having a state of infection identified by claim 56 wherein the genes upregulated are Accession number D87451 - ring finger protein 10; Accession number AL049975, Unknown; Accession number U39067, eukaryotic translation initiation factor 3 subunit 2; Accession number AK000942, Unknown; Accession number AB040057, serine/threonine protein kinase MASK; Accession number AB020719, KIAA0912 protein; Accession number AB007856, FEM-1-like death receptor binding protein; Accession number AL137376, Unknown; Accession number AL137730, Unknown; Accession number M90696, cathepsin S; Accession number AK001143, Unknown; Accession number AF038406, NADH dehydrogenase; Accession number AK000315, hypothetical protein FLJ20308; Accession number M54915, pim-1 oncogene; Accession number D29011, proteasome subunit beta type 5; Accession number AL034348, Unknown; Accession number D87076, KIAA0239 protein; Accession number AJ001403, tracheobronchial mucin 5

subtype B; Accession number J03925, integrin alpha M, Rho-associated kinase 2 (NM\_004850), PTD017 protein (AL050361) unknown genes (AK001143, AK034348, AL049250, AL16199, AL031983), retinoic acid receptor (X06614), G protein-coupled receptors (Z94155, X81892, U52219, U22491, AF015257, U66579) chemokine (C-C motif) receptor 7 (L31584), tumor necrosis factor receptor superfamily member 17 (Z29575), interferon gamma receptor 2 (U05875), cytokine receptor-like factor 1 (AF059293), class I cytokine receptor (AF053004), coagulation factor II (thrombin) receptor-like 2 (U92971), leukemia inhibitory factor receptor (NM\_002310), interferon gamma receptor 1 (AL050337), or any combination thereof.

82. The method of claim 32, wherein the chemokines include CXCR4, CXCR1, CXCR2, CCR2, CCR4, CCR5, CCR6, MIP-1 alpha, MDC, MIP-3 alpha, MCP-1, MCP-2, MCP-3, MCP-4, MCP-5, and RANTES.

83. The method of claim 33, wherein the cell differentiation factors include TGF $\beta$  inducible early growth response 2 (AI473938), zinc finger proteins (AF061261, U00115, X78924), and transcription factors (U31556, AL137681, X68560).

84. A compound of claim 38, wherein the compound modifies kinase activity.

85. A compound of claim 84, wherein the kinase is selected from MAP kinase kinase 3 (D87116), MAP kinase kinase 6 (H07920), MAP kinase kinase 5 (W69649), MAP kinase 7 (H39192), MAP kinase 12 (AI936909), MAP kinase-activated protein kinase 3 (W68281), or MAP kinase kinase 1 (L11284).

86. A compound of claim 21, wherein the compound decreases proteasome subunit expression.

87. A compound of claim 86, wherein the proteasome subunit includes polynucleotides with accession numbers D11094, L02426, D00763, AB009398, AF054185, M34079, M34079, or AL031177.

88. An isolated cationic peptide that reduces polynucleotide expression of SDF-1 receptor.
89. A method of stimulating innate immunity in a subject comprising administering to the subject a therapeutically effective amount of a peptide as set forth in SEQ ID NO:1-4, 11, 18, 25, 32, 39, 46, 53 or 54, thereby stimulating an immune response.
90. The method of claim 89, wherein the innate immunity is evidenced by monocyte activation, proliferation, differentiation or MAP kinase pathway activation.
91. The method of claim 90, wherein the MAP kinases are MEK and/or ERK.
92. The method of claim 89, further comprising administering GM-CSF to the subject.
93. A method of stimulating innate immunity in a subject having or at risk of having an infection comprising administering to the subject a sub-optimal concentration of an antibiotic in combination with a peptide as set forth in SEQ ID NO:1-4, 7, 11, 18, 25, 32, 39, 46, 53 or 54.